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The battle against tuberculosis (TB) is finally becoming a good news story. Worldwide, the 2015 Millennium Development Goal of halting and reversing TB incidence has been achieved globally in most countries, and Canada continues to have one of the lowest TB rates in the world. Globally the proportion of new cases with multidrug-resistant TB (MDR-TB) remains at 3.5%. While some countries have much higher MDR-TB rates, in Canada our rate is 1.1%. Nonetheless, the battle is not over. As we mark World TB day on March 24, 2015 it is useful to consider innovations to help the populations in Canada who are at risk of infection and continue best practices to minimize drug resistance.

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Upcoming conference

April 16–18, 2015. Association of Medical Microbiology and Infectious Disease (AMMI) Canada. Annual Conference, Charlottetown, Prince Edward Island.
http://ammi.ca/annual-conference/2015/

Useful links

Public Health Agency of Canada. **Tuberculosis Prevention and Control in Canada: A Federal Framework for Action.** 2014.
http://www.phac-aspc.gc.ca/tbpc-latb/pubs/tpc-pct/index-eng.php

World Health Organization. **Global tuberculosis report 2014.**
http://www.who.int/tb/publications/global_report/en/

World Health Organization. **Drug-resistant TB: Surveillance & response. Supplement Global tuberculosis report 2014.**
http://apps.who.int/iris/bitstream/10665/137095/1/WHO_HQ_TB_2014.12_eng.pdf?ua=1

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Canada

A summary of tuberculosis in Canada, 2013

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Abstract

Background: The Public Health Agency of Canada (PHAC) monitors active TB disease through the national collaborative Canadian Tuberculosis Reporting System (CTBRS). PHAC uses TB surveillance data and reports to monitor progress towards achieving Canada's goal of preventing and controlling the transmission of TB, as outlined in *Tuberculosis Prevention and Control in Canada —A Federal Framework for Action*.

Objective: To provide an overview of the preliminary number of reported active (new and re-treatment) TB cases and corresponding incidence rates in Canada for 2013.

Methods: Provincial and territorial public health authorities voluntarily submit data to the CTBRS on an annual basis for all TB cases that meet the case definition for national-level surveillance. These data are analyzed by PHAC; the results of the analysis are validated by the supplying jurisdiction and are published annually as the *Tuberculosis in Canada Pre-release* series.

Results: In Canada, 1,640 new active and re-treatment TB cases were reported in 2013 for an overall incidence rate of 4.7 per 100,000 population. There was little change from preceding years in the overall distribution of cases by sex and age group. Although individuals aged 25 to 34 years old represented the largest percentage of reported cases (16%), the highest incidence rate was observed for those aged 75 years or older. Incidence rates in British Columbia, Manitoba, Saskatchewan, Nunavut, and Northwest Territories were higher than the Canadian rate, with Nunavut showing the highest incidence rate. Foreign-born individuals continue to account for the majority of reported TB cases, but the incidence rate per 100,000 population remains highest among Canadian-born Aboriginal people.

Conclusion: Preliminary data from 2013 indicate that there were no notable changes in the number of reported cases of TB or in the overall incidence rate in Canada when compared with previous years' data. Similarly, no changes were noted in the distribution of cases by province or territory, age group or sex.

Introduction

The Public Health Agency of Canada (PHAC) provides national leadership related to public health aspects of tuberculosis (TB) and works collaboratively with domestic and international partners to address TB prevention and control. Two of the key responsibilities of PHAC are the monitoring of and reporting on TB disease through a national surveillance system, the Canadian Tuberculosis Reporting System (CTBRS) which is a collaborative effort with the provincial and territorial ministries of health.

Every year PHAC publishes a brief summary report, *Tuberculosis in Canada—Pre-release* (1) which facilitates timely availability of national-level surveillance data on TB. Every three years, a comprehensive surveillance report is published on *Tuberculosis in Canada* (2). PHAC uses these TB surveillance data and reports to monitor progress towards achieving Canada's goal of controlling and preventing the transmission of TB, as outlined in *Tuberculosis Prevention and Control in Canada—A Federal Framework for Action* (3).

This article provides an overview of the preliminary number of reported active (new and re-treatment) TB cases and corresponding incidence rates in Canada for 2013 (2).

Background

As tuberculosis is legally reportable in all provinces and territories, health care practitioners are legally required to report cases to the provincial or territorial ministry of health. TB has been notifiable in Canada since 1924, which means that it has been prioritized for monitoring at the national level; however, there are no laws in place requiring provinces or territories to report case and outcome data for surveillance purposes to the national level., However, in a cooperative effort to understand the burden of TB in Canada, provincial and territorial public health authorities voluntarily submit data on TB cases that meet the case definition for national-level surveillance (See text box below) (4).

National case definition for tuberculosis (TB) and re-treatment case definition

Tuberculosis

Confirmed Case

- **Laboratory confirmed case:** Cases with *Mycobacterium tuberculosis* complex demonstrated on culture, specifically *M. tuberculosis, M. africanum, M. canetti, M. caprae, M. microti, M. pinnipedii* or *M. bovis* (excluding *M. bovis* Bacillus Calmette-Guérin [BCG] strain).
- **Clinically confirmed case:** In the absence of culture proof, cases clinically compatible with active TB that have, for example:
  - I. chest X-ray changes compatible with active TB;
  - II. active non-respiratory TB (meningeal, bone, kidney, peripheral lymph nodes, etc.);
  - III. pathologic or post-mortem evidence of active tuberculosis;
  - IV. favourable response to therapeutic trial of anti-tuberculosis drugs.

New and Re-treatment Cases of Tuberculosis

- **New cases**

  No documented evidence or adequate history of previously active tuberculosis

- **Re-treatment case**

  I. Documented evidence or adequate history of previously active tuberculosis that was declared cured or treatment completed by current standards; and
  II. At least six months have passed since the last day of previous treatment; and
  III. Diagnosed with a subsequent episode of TB that meets the case definition for active TB.

  OR

  I. Documented evidence or adequate history of previously active TB that cannot be declared cured or treatment completed by current standards; and
  II. Inactive for six months or longer after the last day of previous treatment; and
  III. Diagnosed with a subsequent episode of TB that meets the case definition for active TB.

  OR

  I. Documented evidence or adequate history of previously active TB that cannot be declared cured or treatment completed by current standards; and
  II. Inactive for six months or longer after the last day of previous treatment; and
  III. Diagnosed with a subsequent episode of TB that meets the case definition for active TB.

Methods

Managed by PHAC, the CTBRS is a national case-based surveillance system which maintains selected non-nominal data on people diagnosed with active TB disease including, but not limited to, demographics (e.g., age,

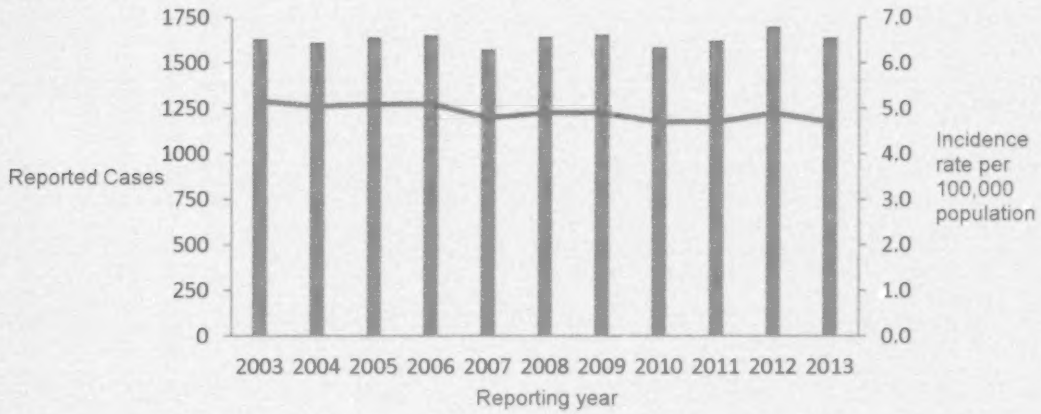
sex, origin, immigration status), and clinical, diagnostic, and treatment information. Risk factor information (e.g., HIV status) and treatment outcome details were gathered, but are not included in this article.
The data are collected either through manual completion of a standard reporting form or by electronic transmission.

TB "incidence rate" is defined here as the number of individuals newly diagnosed with active TB disease (new and re-treatment cases) within each reporting year, per 100,000 population. Rates are expressed as the number of cases reported each calendar year per 100,000 population. No statistical procedures were used for comparative analyses, nor were any statistical techniques applied to account for missing data. Incidence rates in the foreign-born population are based on population estimates derived from the Canadian census. Canadian-born non-Aboriginal is calculated as the total Canadian population, minus the foreign-born population, minus the total Aboriginal population. The diagnostic classification of TB in Canada is based upon the *International Classification of Diseases*, 9th and 10th editions (5, 6).

Results

In Canada, 1,640 new active and re-treatment TB cases were reported in 2013, for an overall incidence rate of 4.7 per 100,000 population which is marginally lower than both the number of TB cases reported in 2012 (n=1,699) and the incidence rate for 2012 (4.9 per 100,000 population). The annual TB incidence rate for Canada has remained below 5 per 100,000 since 2007 (**Figure 1**).

Figure 1: Reported number of tuberculosis cases and incidence rate per 100,000 population, Canada, 2003–2013



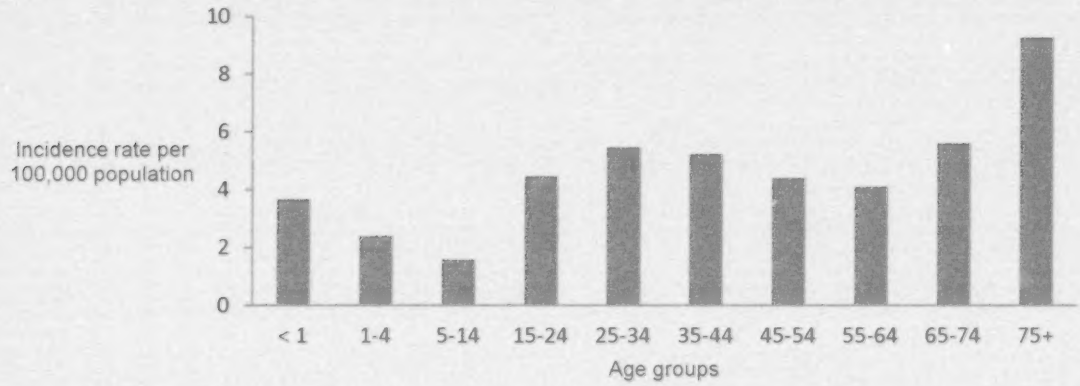
Active TB disease is classified as either respiratory or non-respiratory. Respiratory TB includes pulmonary TB, TB of the pleura, the intrathoracic or mediastinal lymph nodes, or of the larynx, nasopharynx, nose or sinuses. Non-respiratory TB refers to all other disease sites (3). Similar to recent years, in 2013, 77% of cases were diagnosed with respiratory TB and 23% with non-respiratory TB (miliary, central nervous system, peripheral lymph nodes, and other).

Age and sex distribution

In 2013 as in previous years, males accounted for the majority of reported cases at 55% for an overall incidence rate of 5.2 per 100,000 male population. In comparison, females accounted for 45% of all reported cases for a rate of 4.2 per 100,000 female population.

In 2013, individuals aged 25 to 34 years old represented the largest percentage of reported cases at 16%. Seven percent of reported cases were less than 15 years of age. The highest incidence rate was observed for those aged 75 years and older, at 9.3 per 100,000 population (**Figure 2**).

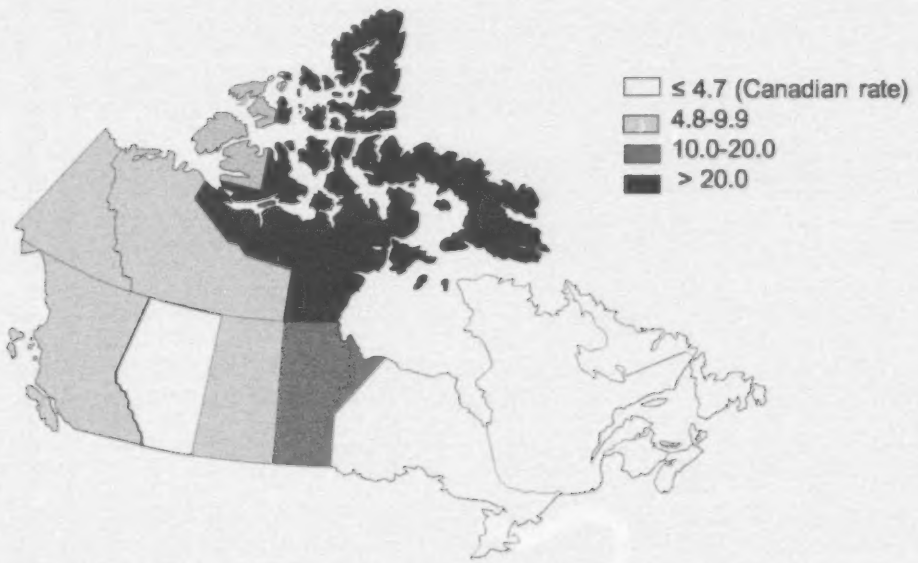
Figure 2: Tuberculosis incidence rate per 100,000 population, by age group, Canada, 2013



Geographic distribution

In 2013, there were no TB cases reported in Prince Edward Island. The incidence rates in the other Atlantic Provinces, as well as in Alberta, Ontario and Quebec, were all equivalent to or below the Canadian rate of 4.7 per 100,000 population (**Figure 3**). The incidence rates in British Columbia, Manitoba, Saskatchewan, Nunavut, Northwest Territories, and Yukon were higher than the Canadian rate. Nunavut continued to show the highest incidence rate at 143.3 per 100,000 population. Since 2004, the incidence rate in Nunavut has remained the highest of any region in Canada, peaking in 2010 at 299.8 per 100,000 population. The 2013 incidence rate for Nunavut was lower than the 2012 rate of 230.5 per 100,000 population; this drop in the rate corresponded to 29 fewer cases reported in 2013 compared with 2012.

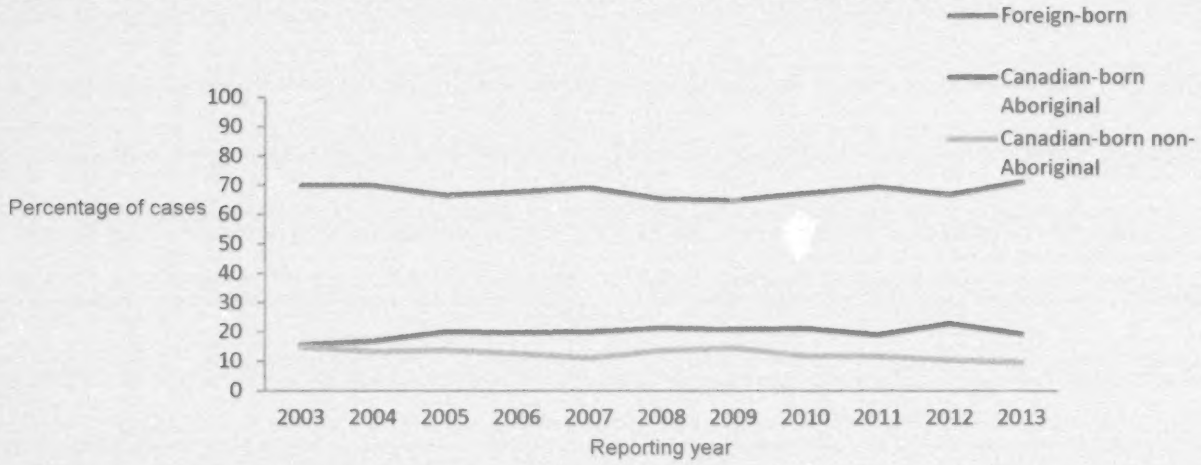
Figure 3: Tuberculosis incidence rate per 100,000 population by province/territory, Canada, 2013



Distribution by origin

Foreign-born individuals and Canadian-born Aboriginal people continued to be disproportionately represented among reported cases of TB in 2013. Data on origin was available for 1,611 (98%) of the 1,640 cases reported in 2013. The foreign-born population, which represented approximately 22% of the total Canadian population in 2013, accounted for 71% of reported cases of known origin (n=1,146), with a corresponding incidence rate of 14.8 per 100,000 population. Canadian-born Aboriginal people made up 4% of the total Canadian population in 2013 but accounted for 19% (n=309) of reported cases of known origin, with a corresponding incidence rate of 19.9 per 100,000 population. Canadian-born non-Aboriginal people accounted for the lowest percentage of reported cases at 10% (n=155), with a corresponding incidence rate of 0.6 per 100,000 population (**Figure 4**).

Figure 4: Percentage of reported tuberculosis cases by origin, Canada, 2003–2013



Canadian-born Aboriginal people comprise three distinct populations: First Nations, Inuit, and Métis. In 2013, of the 309 reported Canadian-born Aboriginal cases, 200 (65%) were First Nations, 91 (29%) were Inuit, and 18 (6%) were Métis. The incidence rate among the Métis was 3.3 per 100,000 population, which was lower than the overall Canadian incidence rate of 4.7 per 100,000 population. By comparison, the incidence rate in First Nations, at 21.8 per 100,000 population, was almost five times the overall Canadian rate. The highest incidence rate, however, was in Inuit, at 154.2 per 100,000 population.

Discussion

Overall, Canada has one of the lowest overall TB rates in the world. Compared with 2012, preliminary data from 2013 indicate that there were no notable changes in the number of reported cases of TB or in the overall incidence rate in Canada. Similarly, no changes were noted in the distribution of cases by province or territory, or by age group or sex. Foreign-born individuals continued to account for the majority of reported TB cases, but the incidence rate per 100,000 population remained highest among Canadian-born Aboriginal people.

There are several factors that need to be considered when interpreting this data. The CTBRS is a passive surveillance system relying on data collected retrospectively from medical and laboratory records. As a result, it is difficult to ascertain whether all people with TB disease are being identified. However, the WHO estimates that Canada's surveillance system has a case detection rate of 92% with a range of uncertainty of 85% to 100% (7).

The surveillance data in this report may be subject to the occasional coding, reporting and processing errors. In general, for the reported cases data on demographic, clinical and laboratory variables are complete for over 95% of reported cases. Some provincial and territorial TB program reporting systems are unable to separately report cases that are First Nations without status from cases that are Métis. Therefore, incidence rates for the Métis should be interpreted with caution.

Finally, the findings from this analysis are provisional. Updated case counts and incidence rates for 2013 will be presented in the next iteration of the *Tuberculosis in Canada* surveillance report.

In conclusion, a comprehensive understanding of the epidemiological trends of TB across Canada is integral to monitoring progress toward the goal of a reduced national TB burden. As the epidemiology of TB in Canada and the world evolves, PHAC will continue to work with its partners to improve the quality and nature of the data and report on it in a timely manner.

Acknowledgments

The Surveillance and Epidemiology Division at the Public Health Agency of Canada would like to acknowledge the provincial and territorial tuberculosis programs and their teams for their contribution to and participation in the Canadian Tuberculosis Reporting System (CTBRS).

Conflict of interest

None

Funding

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A summary of tuberculosis drug resistance in Canada, 2003–2013

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Abstract

Background: Drug-resistant strains of tuberculosis (TB) pose a serious threat to prevention and control efforts. In response to this growing worldwide concern, the Public Health Agency of Canada (PHAC) established and maintains the Canadian Tuberculosis Laboratory Surveillance System (CTBLSS) in partnership with the Canadian Tuberculosis Laboratory Technical Network (CTLTN) and participating laboratories.

Objective: To report on national trends and patterns in anti-tuberculosis drug resistance in Canada for the years 2003 to 2013.

Method: At the beginning of each calendar year, participating laboratories submit to PHAC reports on the results of anti-tuberculosis drug susceptibility testing for all isolates tested during the preceding year. These data are then analyzed by PHAC and the results are validated by supplying laboratories. The results are published annually as the *Tuberculosis Drug Resistance in Canada* series.

Results: In 2013, anti-tuberculosis drug susceptibility test results for 1,380 isolates were reported to PHAC. Of these, 762 (54%) were reported as *Mycobacterium tuberculosis* complex (MTBC) where the species was known. Two thirds (68%) of all the reported isolates originated from the three largest provinces, British Columbia, Ontario and Quebec. Overall, of the laboratory results received, 112 (8.1%) showed resistance to at least one first-line drug and, of these, the majority (93 or 83%) were monoresistant.

Conclusion: TB drug resistance observed in Canada remains well below the global average. Over the last 10 years, the percentage of isolates with resistance to one or more of the first-line medications has decreased from 10.5% in 2003 to 8.1% in 2013.

Introduction

Drug-resistant strains of tuberculosis (TB) pose a serious threat to prevention and control efforts. Although drug-resistant TB has not yet been identified as a major problem in Canada, its potential to become an issue is high because of the frequency with which Canadians travel abroad.

In 1998, in response to a growing concern about TB drug resistance worldwide, thegovernment of Canada , in partnership with the Canadian Tuberculosis Laboratory Technical Network (CTLTN)—a network of provincial and territorial TB laboratories across Canada with representation from their respective technical or scientific TB programs leads—established the Canadian Tuberculosis Laboratory Surveillance System (CTBLSS) to monitor trends and patterns in tuberculosis drug resistance in Canada over time. This article provides an overview of the most recent data on TB drug resistance in Canada as well as details on the overall level of TB drug resistance in Canada for the period 2003 to 2013, focusing, in particular, on 2013 (1).

Background

The CTBLSS is an isolate-based surveillance system designed to collect timely data on TB drug resistance across Canada. Information on the results of all unique isolates tested for drug resistance during the previous calendar year are voluntarily submitted by provincial TB laboratories to PHAC for inclusion in the CTBLSS. The primary objectives of the CTBLSS are:

- To describe the number of drug-resistant TB isolates in Canada on an annual basis by resistance pattern and by originating province/territory, and by sex and age.
- To monitor trends in drug-resistant TB in Canada over time by originating province/territory, and by sex and age.

TB drug resistance is determined through susceptibility testing of cultures grown from clinical specimens obtained from individuals with culture-positive TB (2). People with active TB disease are said to have drug-resistant TB if the strain of *Mycobacterium tuberculosis* complex (MTBC) causing their disease is resistant to one or more of the four first-line anti-TB drugs, isoniazid, rifampin, ethambutol or pyrazinamide. Data are submitted for confirmed cases of MTBC, including *Mycobacterium tuberculosis*, *M. africanum, M. canetti, M. caprae, M. microti, M. pinnipedii* or *M. bovis*, but excluding *M. bovis* Bacille Calmette-Guérin (BCG). See text box below for definitions of the different drug-resistant patterns.

Definitions of different drug-resistant patterns to tuberculosis

Monoresistance

- Resistance to only one first-line anti-TB drug

Polyresistance (other patterns)

- Resistance to more than one first-line anti-TB drug, not including the isoniazid and rifampin combination of MDR-TB

Multidrug-resistant tuberculosis (MDR-TB)

- TB due to bacteria resistant to isoniazid and rifampin with or without resistance to other anti-TB drugs

Extensively drug-resistant TB (XDR-TB)

- TB due to bacteria resistant to isoniazid and rifampin and any fluoroquinolone and at least one of the three injectable second-line anti-TB drugs (amikacin, capreomycin or kanamycin)

Methods

At the beginning of each calendar year, participating laboratories voluntarily submit drug susceptibility testing (DST) results for all MTBC isolates tested in the previous year. Although some laboratories report results for *M. bovis* BCG strain, these are excluded from this article.

The following information is submitted to PHAC: the date the isolate or specimen was received at the laboratory and its identification number; the province/territory where the isolate was tested in the province or territory where it originates from; the sex, date of birth (or age) of the person the isolate came from; and the drug susceptibility results.

With respect to DST results, participating laboratories are asked to submit test results for all first-line anti-TB drugs (isoniazid [INH], rifampin [RMP], ethambutol [EMB] and pyrazinamide [PZA]). If isolates show resistance to isoniazid and rifampin, second-line drug testing should be done to rule out XDR-TB (2). Laboratories are requested to report on the DST results for a fluoroquinolone (ofloxacin, moxifloxacin or levofloxacin) and the injectable agents (amikacin, kanamycin and capreomycin).

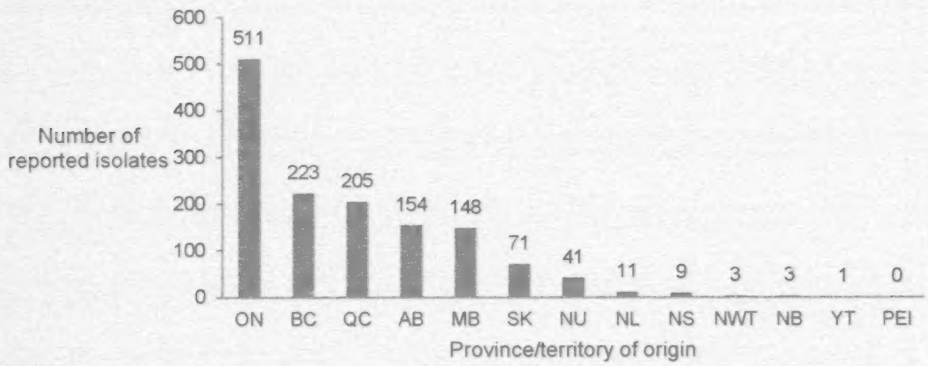
The analysis presented here is based on descriptive statistics only. No statistical procedures were used for comparative analyses, nor were any statistical techniques applied to account for missing data. Data in tables with small cell sizes (n≤5) were not suppressed, since disclosure is not deemed to pose any risk of identifying individual cases. These procedures are in line with PHAC's *Directive for the collection, use and dissemination of information relating to public health* (3).

Results

Reporting for 2013

In 2013, TB DST results for 1,397 isolates were reported to PHAC. Of these, 762 (54%) were reported as MTBC where the species was known (750 were *M. tuberculosis*; 8 were *M. africanum* and 4 were *M. bovis*) and 618 (44%) were MTBC of an unknown species. Seventeen (1.2%) isolates were identified as *M. bovis* BCG and were excluded from further analyses (data not shown). As a result, laboratory results for 1,380 isolates were analyzed for this article. Of these, 68% of all the reported isolates originated from the three largest provinces, British Columbia, Ontario and Quebec. **Figure 1** provides a breakdown of the number of isolates tested by province or territory of origin of the isolate.

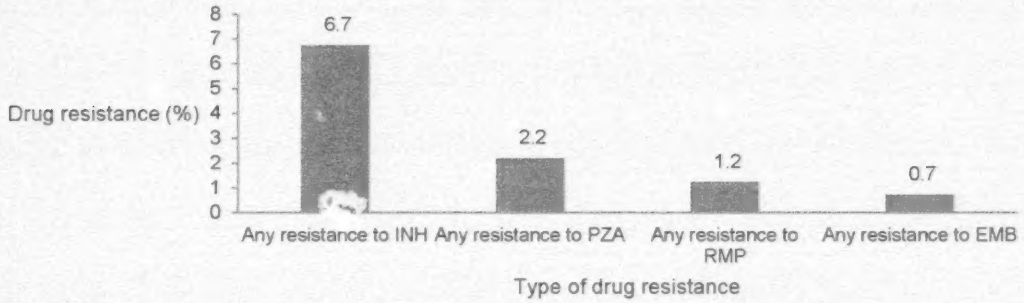
Figure 1: Number of *Mycobacterium tuberculosis* complex isolates tested by province or territory of origin, Canada, 2013



Monoresistance

In 2013, of the 112 TB isolates reported to be resistant to at least one of the four first-line drugs, the majority, 93 (83%), were monoresistant. Of these, 74 (80%) were isoniazid-resistant, 17 (18%) were pyrazinamide-resistant, and 2 (2%) were rifampin-resistant. No isolates were identified as ethambutol-monoresistant. **Figure 2** provides a breakdown of the percentage of all the isolates tested that showed any resistance to one of the four first-line TB drugs.

Figure 2: Reported tuberculosis drug resistance in Canada by first-line drug, 2013



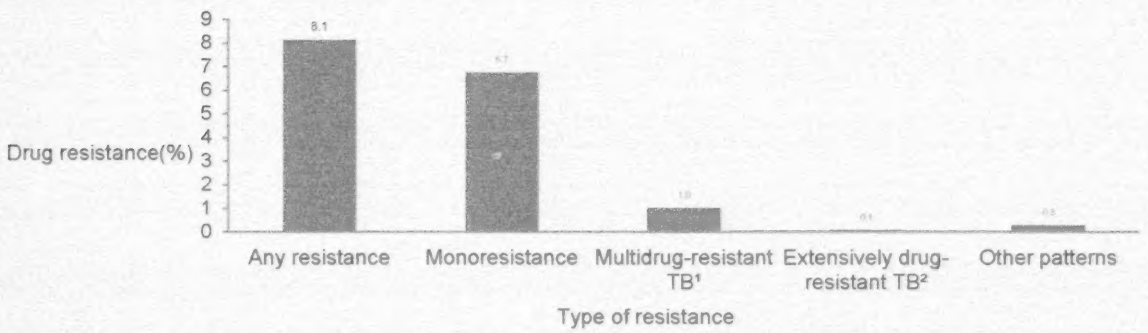
Multidrug-resistance

In 2013, fifteen isolates were resistant to bothisoniazid and rifampin (classifying these isolates as MDR-TB at least), six (40%) of which were resistant only to isoniazid and rifampin. In addition to being resistant to isoniazid and rifampin, three of these fifteen (20%) were also resistant to ethambutol, one (6%) to pyrazinamide, and five (33%) to all first-line drugs. An additional four isolates (0.3%) were resistant to two or more of the first-line drugs excluding the isoniazid and rifampin combination.

Extensively drug-resistance

To rule out XDR-TB, all fifteen isolates that were resistant to both isoniazid and rifampin were subsequently tested for resistance to select second-line drugs. Of these, twelve isolates were susceptible to both the injectable agents and the fluoroquinolones, one was resistant to an injectable, and one was resistant to a fluoroquinolone. As a result, these fourteen isolates (1.0% of all isolates tested) were classified as MDR-TB. The remaining isolate was resistant to at least one of the injectables and to a fluoroquinolone, which classified it as XDR-TB (0.1% of all isolates tested). Thus, results from additional second-line testing in 2013 identified fourteen isolates as MDR-TB and one as XDR-TB (**Figure 3**).

Figure 3: Patterns of reported TB drug resistance as a percentage of isolates tested, 2013



[1] Multidrug-resistant TB (MDR-TB) is TB that is resistant to at least isoniazid and rifampin, but which does not meet the definition of XDR-TB.
[2] Extensively drug-resistant TB (XDR-TB) is TB that is resistant to at least the two best first-line drugs, isoniazid and rifampin, plus resistant to second-line drugs, including any fluoroquinolone and at least one of three injectable agents, amikacin, capreomycin and kanamycin.

Geographic distribution

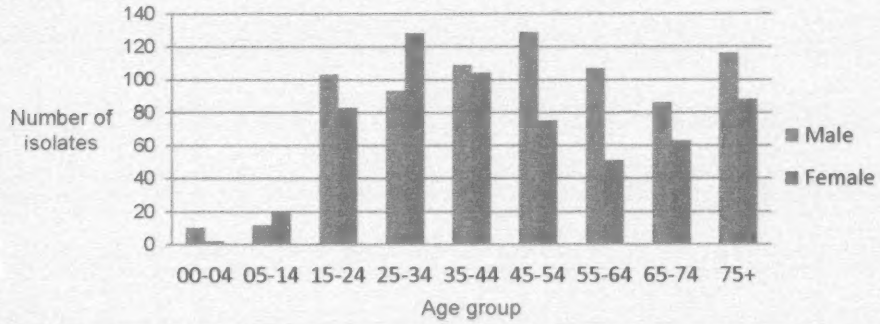
In 2013, 68% of all the reported isolates originated from the three largest provinces, British Columbia, Ontario and Quebec. All isolates from Northwest Territories, Nunavut, Yukon, and Newfoundland and Labrador were fully susceptible to all the first-line drugs tested. Prince Edward Island did not report a case of TB in 2013 and no

laboratory results were reported by that province. Of the 15 isolates resistant to both isoniazid and rifampin in 2013, 13 originated from Ontario and 2 from Quebec.

Demographic data

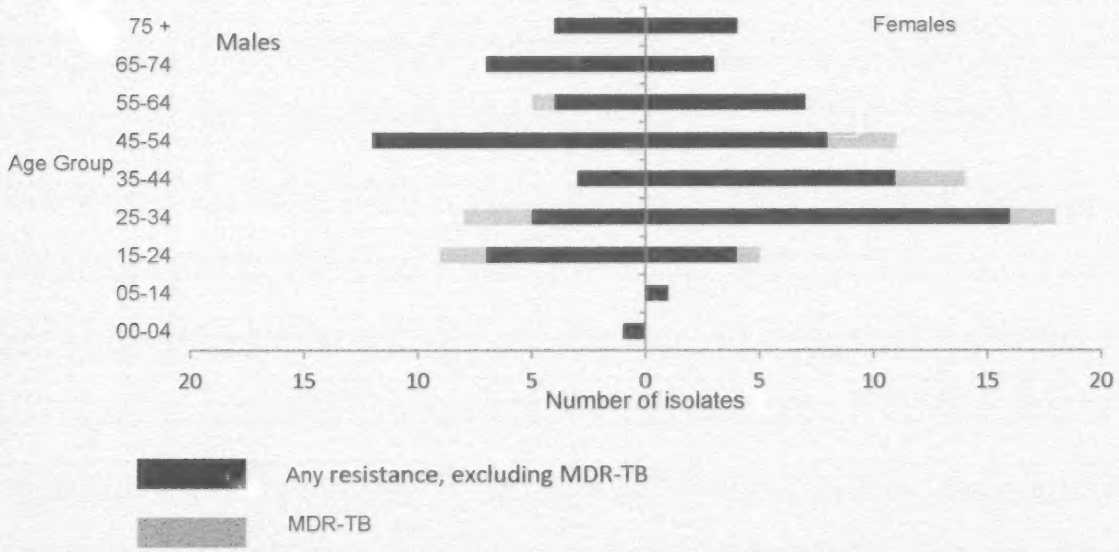
In 2013, sex information was reported for all but two individuals from whom isolates were obtained, and age or date of birth was available for all. Males accounted for 55% of all reports. **Figure 4** shows the number of isolates tested by age group and sex.

Figure 4: All isolates tested by sex and age group, 2013



Of the 112 isolates for which any drug-resistance pattern was identified, 23% were from individuals between the ages of 24 and 34 years and 21% were from individuals 45 to 54 years of age. Less than 2% of isolates were from individuals under 15 years of age. All MDR-TB isolates were from individuals between the ages of 15 and 64 years. There were no MDR-TB cases reported for individuals less than 15 years of age or over 65 years of age. Females accounted for 56% of the isolates showing any resistance and 67% (10/15) of the isolates with resistance to both isoniazid and rifampin. **Figure 5** provides the breakdown of isolates showing any resistance and those MDR-TB isolates by sex and age for 2013.

Figure 5: Number of isolates showing resistance by age group and sex, 2013

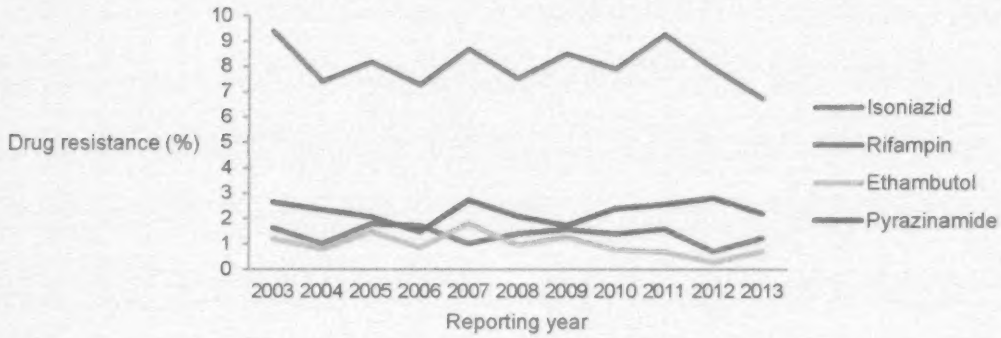


Trends: 2003–2013

For the period 2003 to 2013, DST results were reported for 14,841 isolates. On average 1,349 results were received each year ranging from a high of 1,405 in 2003 to a low of 1,267 in 2007.

Between 2003 and 2013, 8% (range: 6.7%–9.4%) of all isolates tested were isoniazid-resistant. From 2011 to 2013, isoniazid resistance dropped slightly, from 9.2% in 2011 to 7.9% in 2012 and then to an all-time low of 6.7% in 2013. For the period 2003 to 2013, ethambutol, rifampin and pyrazinamide resistance have consistently remained below 3% (**Figure 6**).

Figure 6: Any drug resistance, by type of first-line drug, as a percentage of all isolates tested, 2003–2013

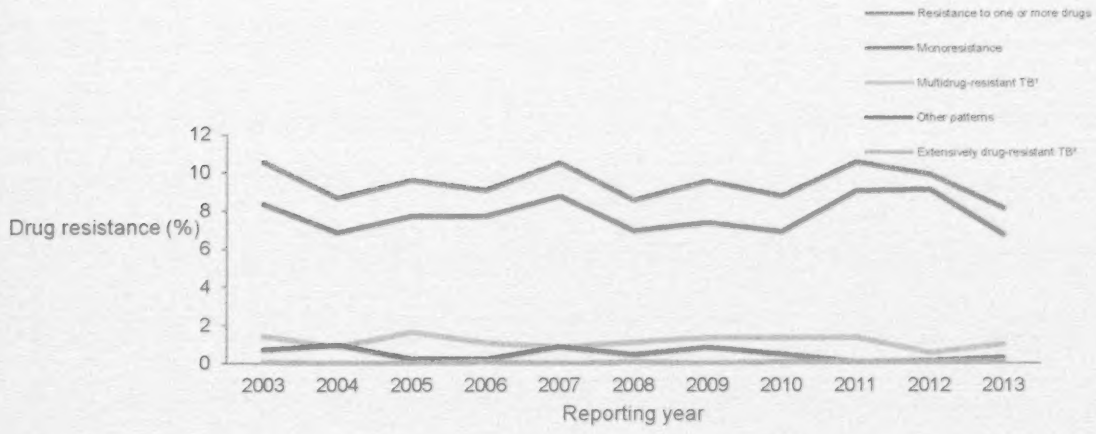


Of all the results reported between 2003 and 2013, 1,399 (approximately 9%) were resistant to one or more of the first-line medications, ranging from a high of 10.5%, reported in 2003, 2007 and 2011, to a low of 8.1% in 2013.

For the period 2003 to 2013, 170 isolates were classified as MDR-TB, representing 1.1% of isolates tested over this time. Seven isolates were classified as XDR-TB, representing an annual average of less than 0.1% of the total number of isolates tested for the period 2003 to 2013. An average of 16 MDR-TB isolates were reported each year, ranging from a high of 22 (1.6% of all isolates tested) in 2005 to a low of 8 (0.6% of all isolates tested) in 2012. For the period 2003 to 2013, all 170 MDR-TB isolates originated from six provinces: Alberta, British Columbia, Manitoba, Ontario, Quebec, and Saskatchewan. Of the additional seven isolates identified as XDR-TB, five were reported from Ontario, one from Manitoba and one from Québec.

Figure 7 shows the overall pattern of reported TB drug resistance as a percentage of isolates tested for the period 2003 to 2013. While there have been small fluctuations in the percentage of isolates showing various resistance patterns, there has been no notable change over this time.

Figure 7: Patterns of reported TB drug resistance as a percentage of isolates tested, 2003–2013



[1] Multidrug-resistant TB (MDR-TB) is TB that is resistant to at least isoniazid and rifampin, but which does not meet the definition of XDR-TB.
[2] Extensively drug-resistant TB (XDR-TB) is TB that is resistant to at least the two best first-line drugs, isoniazid and rifampin, plus resistant to second-line drugs, including any fluoroquinolone and at least one of three injectable agents, amikacin, capreomycin and kanamycin.

Discussion

TB drug resistance in Canada remains well below the global average. Over the last 11 years, the percentage of isolates resistance to one or more of the first-line medications has decreased from 10.5% in 2003 to 8.1% in 2013.

Organisms resistant to both isoniazid and rifampin, a resistance pattern defined as multidrug-resistant TB (MDR-TB); pose a considerable challenge to treatment and prevention efforts because effective anti-tuberculosis drugs are limited. Data published by the World Health Organization (WHO) show that globally, in 2012, about 3.6% (95% CI: 2.1%–5.1%) of new TB cases and 20.2% (95% CI: 13.3%–27.2%) of previously treated TB cases were MDR-TB (4). In Canada, overall MDR-TB rate is 1.1%.

These data need to be considered in light of some limitations. Given the minimal identifying information available for each isolate (age and sex), it is possible that multiple records from one individual could be included in the database. However, this bias is believed to be minimal.

Typically, only isolates with MDR-TB or other extensive resistance patterns will undergo drug sensitivity testing to select second-line drugs. Although the Clinical and Laboratory Standards Institute recommends that isoniazid-monoresistant isolates, as well as other poly-resistant, non-MDR isolates, be tested for second-line drug resistance, this is not universally done in Canada. Other isolates which are not MDR-TB may be resistant to a fluoroquinolone because of the widespread use of these antibiotics for other respiratory infections. To some extent, this limits our understanding of the emergence of second-line resistance within Canada.
The demographic and clinical data collected through the CTBLSS are minimal. As such, no differentiation can be made between primary and secondary/acquired drug resistance, nor can differentiation be made between resistance patterns for new cases versus re-treatment cases. However, the *Tuberculosis in Canada* report also presents case-based data on primary and acquired drug resistance in Canada and, combined with the *Tuberculosis: Drug Resistance in Canada Report*, provides a comprehensive overview of TB-case and drug-resistance surveillance data from a national perspective.

Data collected to date indicate that the presence of TB drug resistance in Canada is below the global average and that it has remained relatively stable since reporting began. With growing worldwide concern about drug

resistance and the emergence of XDR-TB, however, the CTBLSS remains vital to the monitoring of TB drug resistance in Canada.

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Conflict of interest

None

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TB in Canada—The battle is not over

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In this issue of CCDR, Gallant et al. report 2013 data from the Canadian Tuberculosis (TB) Reporting System which suggests that the incidence rate of active TB disease in Canada has not changed when compared to 2012 and has remained stable since 2007 (under 5 per 100,000) (1). Although it is commendable that in Canada the rates of TB have remained low for many years, it should be pointed out that more can be done to bring down the Canadian incidence. The reported incident rate of TB is highest among Canadian-born Aboriginal peoples (19.9 per 100,000) compared to all other groups including the foreign born (14.8 per 100,000); however, in terms of absolute numbers, the foreign-born population has the largest burden of disease (1,146 cases compared to 309 cases) (1). The article also found that the Canadian-born Aboriginal population makes up 4% of the total Canadian population but accounted for 19% of all the cases of active TB disease (1).

The highest incidence rate reported in Canada was recorded in Nunavut at 143 per 100,000 in 2013 (1). The incidence rate of active TB disease in Nunavut has shown a rising trend over the past 10 years and reached 304 per 100,000 in 2010 (representing 101 active cases). Nunavut is part of the Inuit Nunangat (Inuit homeland) which encompasses four regions in the Canadian Arctic. Inuit represent 85% of the population of Nunavut. Inuit have a disproportionately high rate of TB across Canada compared to other Canadian-born Aboriginal peoples. In the Gallant et al article in this issue, the incidence rates reported for Canadian-born Aboriginal peoples for First Nations and Métis were 21.8 per 100,000 and 3.3 per 100,000, respectively; whereas the rate for Inuit (across all regions of the Inuit Nunangat) was 154.2 per 100,000—more than 30 times the Canadian incidence rate (1). It should be noted that although Inuit have the highest incidence, First Nations peoples carry the largest burden of disease in Canada among the Canadian-born Aboriginal population. Furthermore, the reported incidence rate among First Nations has remained stagnant for over a decade while the rate among non-Aboriginal Canadians has steadily declined. The geographic distribution of TB disease among First Nations peoples has been shown recently to be highly focal across the northern portion of the Prairie Provinces and increases from west to east across these regions (2).

These high rates of TB among the Canadian Aboriginal population continue to persist despite dedicated public health programs for the prevention and control of TB based on the *Canadian Tuberculosis Standards* (3). Unique challenges exist in prevention and control of TB among Canadian-born Aboriginal populations, including significant geographic dispersal across large masses of land, health care delivery challenges, the need to provide culturally appropriate care, risk factors, and the prevalence of unequal distribution of social determinants of health related to TB (4).

Important in any approach taken in the prevention and control of TB among Aboriginal people is to engage Aboriginal people directly in the quest for solutions. Homegrown solutions are often the best guided and most sustainable. The national Inuit organization Inuit Tapiriit Kanatami (ITK) developed an Inuit-Specific Tuberculosis Strategy Task Force which included federal, provincial and territorial government agencies (5). The Inuit Specific-TB Strategy outlines a framework and process for partners to develop an Inuit-specific TB action plan, including key elements in community education and mobilization, partnerships towards addressing social determinants of health, and new research aimed at TB prevention and control (5). They outline five core TB action plan components where they put forward many of the specific barriers encountered by Inuit in these regions relating to TB prevention and control. Health Canada and a committee of experts including the Assembly of First Nations developed a strategy against TB to inform TB prevention and control programs that service the First Nations on-reserve (6).

New technologies and approaches for the prevention, diagnosis and treatment of TB being used around the world may also show promise in the specific environments faced by Aboriginal Canadians. Recently published work

done in Nunavut through a collaboration between Nunavut Tunngavik Incorporated (NTI), the Government of Nunavut, and the Ottawa Hospital Research Institute to raise community awareness about TB followed by a door-to-door screening campaign in Iqaluit may contribute to successful control of TB in Aboriginal communities and highlights the strength in Aboriginal participatory research (7). The Xpert® MTB/RIF diagnostic assay, which is an automated, cartridge-based, real-time polymerase chain reaction assay (Cepheid, Sunnyvale, California) for rapid detection of *Mycobacterium tuberculosis* (MTB) disease and rifampin resistance (8), shows significant promise in diagnosing TB earlier in remote regions where no TB laboratory facilities are available and where often the highest burdens of TB disease are seen in Canada. The next generation of whole genome sequencing, a tool that allows the complete DNA of the TB genome to be sequenced, offers significantly better resolution than current methods and has shown significant promise to better understand transmission dynamics in the Aboriginal Canadian population (9, 10). Further research in this area will help further characterize transmission dynamics of the disease in this population. Other technologies such as the interferon gamma release assay (IGRA) for the diagnosis of latent TB infection is a blood test that is not usually affected by the Bacille Calmette-Guérin (BCG) vaccine and was shown to be feasible in the Arctic setting (3,11). Recent evidence involving a large randomized control trial supporting a significantly shortened treatment for latent TB infection, rifapentine and isoniazid (INH), given once a week for 12 weeks was shown to be as effective as nine months of INH (the current standard), also shows significant promise (12). The results have been recently replicated in children as well (13).

Short of discovering a new effective vaccine to prevent TB, we need to find new ways of preventing TB disease in those that have latent infection and interrupting transmission in those that have active TB disease. In addition, innovative ways to reduce the unequal distribution of social determinants of health that drive TB in many Aboriginal Canadian populations are and will continue to be of paramount importance in tackling the disease. Despite the fact that the rates of TB have remained stable for the past several years in Canada, the fight against TB is not over—the battle is not yet won. Renewed investments in research, program development and evaluation that includes performance indicators are needed before we can start talking about eliminating this disease once and for all among Canadian-born Aboriginal peoples.

Conflict of interest

None

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